DETAILED ACTION

Response to Amendment

1. The response filed on **5/13/09** has been entered.

2. Applicant's arguments filed 5/13/09 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1, 4, 7-9, 11-12, 23, 28-32 and 33-36 are pending in this office action.

5. The rejection of claims 1, 4, 7-9, 11-12, 23, 28-32 and 33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn based on Applicant's traversal that examples 1 to 3 provide written description for the ranges between 25-60% of HEC/HMPC.

6. The rejection of claims 1, 4, 7-9 and 12 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn based on the cancellation of the term "selected" from the claims and the changing 0<10% to recite "between 0 and 10%.

7. Claims 1, 4, 7-9, 11-12, 23, 28-31 and 33-36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss (US 4,252,786) in view of Jenkins (US 4,940,587) for the reasons made of record in Paper No. 11/13/08 and as follows.

Applicant argues that "Weiss fails to disclose 1-58% by weight of a mixture of hydroxyethyl cellulose and hydroxypropyl methylcellulose provided as a homogenous mixture with the other tablet ingredients, as recited in the amended claims" and that the "hydroxypropyl methylcellulose described in Weiss is provided as a part of a coating solution, which is applied to the tablet, and is not a part of the matrix".

Applicant also argues that Jenkins fails to remedy the deficiencies of Weiss and contrary to the Examiner's statement; Jenkins does not provide a mixture of hydroxyethyl cellulose and hydroxypropyl methylcellulose.

In response as summarized below, although Weiss teaches the combination of hydroxyethyl cellulose and hydroxypropylmethyl cellulose, they do not teach the recited combined concentration; however Jenkins teaches the same polymer mixture "Natrosol 250" as described in the instant specification. Thus it is reasonable to assume the "Natrosol 250" comprises the percentages required for hydroxyethyl cellulose and hydroxypropyl methylcellulose (as required by claims 1, 9, 23, 30, 33, 34-37). It should be noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would

have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In summary, Weiss teaches with regards to instant claims 1, 4, 8-9, 23 30 and 33 (in parts), a rate release medicament (i.e., a controlled release tablet) comprising polymers of acrylic acid cross linked with polyalkenyl alcohols less than 50% (such as Carbopol 934; the same agent employed in Example 1 of the specification page 7, line 15) (as in claims 1 4 and 7, see col. 2, lines 40-46), wherein the composition comprises hydroxymethyl cellulose, hydroxypropyl methyl cellulose, talc and ethyl cellulose. Also see table 3, col. 6, lines 8-24 as required by instant claims 1 and 8-9 wherein the granulating and tableting aids are taught see col. 3, lines 25-55.

The active agent is assumed to comprise more than 1% of medicament based upon col. 2, lines 64-68 and also col. 5 and 6 Examples 1 and 3-5 (as required by instant claim 1). Weiss teaches the formulation comprises granulating procedures and tableting aids (see col. 3, lines 25-55). Although the percentages are not taught it is assumed that these agents (diluents, lubricants etc.) are between 0-95% since these agents in tablet formulation are the bulk constituents of a tablet. Weiss further teaches that the composition is film coated with cellulose esters (see col. 5-6 examples 1 and 3) wherein the film coating material is reasonably about 0.5-50% (see col. 6, line 35-36 as required by instant claims 7 and 28). Weiss also teaches that the formulation may contain lactose and microcrystalline cellulose (see col. 3, lines 29-31 as required by instant claim 28 and 31). Weiss then teaches that the composition is granulated.

Therefore because homogenous mixtures are routinely made in the art, the limitations of instant claims 1, 23 and 33 are reasonably anticipated. Weiss also teach the controlled release composition comprises 5% HMPC (see col. 6, lines 18-19, as required by instant claim 35).

However Weiss is silent in teaching the specific mixture of hydroxyethyl cellulose and hydroxypropylmethyl cellulose at the recited concentrations. Nor does Weiss teach the claimed medicaments of instant claim 11.

Jenkins is added to show that in a sustained (i.e., a controlled) release tablet the mixture of hydroxyethyl cellulose and hydroxypropycellulose is well known in the pharmaceutical controlled release art. Jenkins teaches that in a controlled release drug formulation the level of the hydroxyalkyl cellulose serves to control the release of the drug and the preferable mixture is hydroxypropylmethyl cellulose and hydroxyl ethyl cellulose (i.e., Natrosol 250 HX, which is same as Applicants example 1 in the specification) and may contain between 2-15%, which is within the recited percentage 1-58% as required by instant claims 1, 9, 23, 30 and 33. Therefore since the same agent is employed, it is assumed that the composition comprises 1-25% of hydroxyethyl cellulose and 1-35 % of hydroxypropyl methylcellulose (as required by instant claim 16, see Examples 1, 7 and 8). Jenkins further teaches the medicament maybe morphine or ibuprofen in a percent ratio of more than 1%, (see col. 3, lines 18-20 and col. 5, lines 66-67 as required by instant claims 1, 9, 23, 30 and 33).

However Jenkins fails to teach the composition comprises 1-50% polymers of acrylic acid crosslinked with a polyalkenyl alcohol (as required by instant claim 1)

One of ordinary skill in the art would have been motivated to combine the Weiss and Jenkins teachings to formulate a controlled release drug that comprises an acrylic acid cross linked with polyalkenyl alcohol (Carbopol 934), comprising 2-15% of hydroxypropylmethyl cellulose and hydroxyethyl cellulose in a matrix with magnesium stearate and talc because these agents are well known in the art for formulating a controlled release drug. As discussed above by Jenkins, the level of the hydroxyalkyl cellulose serves to control the release of the drug, therefore based on the desired predetermined rate, one would choose a mixture of the hydroxyalkyl cellulose based upon the rate of dissolution. Also, it is known in the art that the higher aliphatic alcohol, together with the water soluble hydroxyalkyl cellulose, serves to control the release of the drug from the composition. The level of alcohol in the composition will therefore be determined by the rate of drug release required. Generally, however, the composition will contain between 5% and 35% (w/w), especially 10% and 30% (w/w), (as a proportion of the total dosage form weight) of the higher aliphatic alcohol). See Jenkins col. 2, lines 45-52. Also, controlled release formulations are well known in the art, wherein mixing hydrophilic and hydrophobic polymers to have the required or desired release pattern is very well known in the art. One of ordinary skill in the art would have been motivated to identify among the varying polymers which combination would give the desired controlled release pattern, since it is well known in the art that the aim of these controlled release pharmaceutical formulations is to substantially approach zero

order release. It is within the purview of the skilled artisan to optimize the combination of these hydrophilic and hydrophobic polymers based on the knowledge of the prior art in approaching zero order release.

Accordingly all the components required for a controlled release formulation are taught in the prior art. One of ordinary skill in the art would have been motivated to formulate a controlled release pharmaceutical based on the teaching of the prior art to include all the necessary agents because the terms "controlled release" and "delivery" are used in their broadest sense to include mechanisms such as diffusion, chemical and enzymatic reactions, dissolution, osmosis, targeting, as well as the utilization and manipulation of biological processes when this drug is in the system. Much of the relevant literature is very precise in that it either concentrates, for example, on a specific type of polymer offering suitable transport characteristics for an individual permeant, or concentrates on a range of permeants transported through a single polymer type, or concentrates on a unique application. Therefore one of ordinary skill in the art would be motivated to explore which of the polymers known in the art would yield a better controlled release delivery of the drug.

Thus it is within the purview of the skilled artisan to optimize based on the prior art knowledge. It is the Examiners position that once the concept is known or available, one of ordinary skill in the art would be motivated to find the optimum working range. Also it has been held that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine. See In re Aller, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955). In conclusion, the

combination of both Weiss and Jenkins make it obvious to one of ordinary skill in the art to make and use the claimed invention at the time of filing the instant application.

8. Applicant's request that the Double Patenting rejection be held in abeyance until it is made permanent is noted but will be maintained in this Office Action and future Office Actions until withdrawn. Since this is not the only rejection remaining, the double patenting rejection is therefore maintained below.

Claims 1, 4, 7-9, 11-12, 23, 28-31 and 33-36 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1 - 22** of U.S. Patent Application No. **11/473,386** for the reasons made of record in Paper No. 11/13/08 and as follows.

9. Claims 1, 4, 7-9, 11-12, 23, 28-31 and 33-36 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1 - 28** of U.S. Patent No. **7090867** for the reasons made of record in Paper No. 11/13/08 and as follows.

10. The affidavit filed on 5/13/09 by Isa Odidi and Amina Odidi under 37 CFR 1.132 has been considered but is ineffective to overcome the claim rejections set forth.

Declarant argues that Weiss teaches “a two-step process to make a controlled release dosage form containing two compartments. The first is an inner compartment

made of a matrix core containing the drug and the second is an outer coating made of a polymer film coat comprising a combination of polymers to modify the drug release rate".

In response Declarant should note that the rejection is a 103 rejection and not a 102 rejection. Even though Weiss teaches the formulation in compartments, Jenkins teaches the formulation without compartments. Thus the skilled artisan would have reasons to combine the teachings of Weiss and Jenkins with a reasonable expectation of success in doing so.

The showing of Tables 1-4 is given careful consideration, however found not persuasive because Jenkins specifically teaches that the "level of alcohol in the composition will therefore be determined by the rate of drug release required. Generally, however, the composition will contain between 5% and 35% (w/w), especially 10% and 30% (w/w), (as a proportion of the total dosage form weight) of the higher aliphatic alcohol". See Jenkins col. 2, lines 45-52.

Declarant admits that the "tablets according to the present invention and those according to the teaching of Weiss et al. contain the same type of ingredients in the same amounts, except that in the case of the Weiss et al. tablets, hydroxyethyl cellulose and hydroxypropylmethyl cellulose are not in a homogenous blend with the rest of the materials that make up the Weiss tablets, i.e., they are in a separate compartment".

In response, it is within the skilled artisan to modify the Weiss composition by incorporating Jenkins formulation to result in the claimed invention.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. V. G./
Examiner, Art Unit 1618

/Robert C. Hayes/
Primary Examiner, Art Unit 1649